



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,710	01/22/2002	Koichi Masuda	047940-0119	5419
23524	7590	05/03/2004	EXAMINER	
FOLEY & LARDNER 150 EAST GILMAN STREET P.O. BOX 1497 MADISON, WI 53701-1497			DAVIS, RUTH A	
			ART UNIT	PAPER NUMBER
			1651	

DATE MAILED: 05/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary**Application No.**

10/054,710

Applicant(s)

MASUDA ET AL.

Examiner

Ruth A. Davis

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 15, 16, 31 and 32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14, 17-30 and 33-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10-2003</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's Request for Continued Examination and amendment filed February 17, 2004 has been received and entered into the case. Claims 1 – 35 are pending; claims 15 – 16 and 31 – 32 are withdrawn from consideration; claims 1 – 14, 17 – 30 and 33 – 35 have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 112

Rejections under 35 U.S.C. 112, second paragraph, have been withdrawn.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

Art Unit: 1651

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1 – 8, 10, 14, 17 – 24, 26, 29 – 30 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kai in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof, wherein the matrix is capable of being rapidly degraded losing about half of its proteoglycan content within 24 hours when treated with IL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc³ aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal,

Art Unit: 1651

epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring is performed without addition of extrinsic radioactivity and the method further comprises identifying one or more test agents that have desirable characteristics and producing the agents as a therapeutic drug. The modulator of the ECT tissue is a matrix stimulating agent, cytokine or TNF-alpha wherein the cytokine is interleukin 1 (IL-1).

Kai teaches a method for determining effects of agents on cartilage, wherein the cartilage is cultured with IL-1 or TNF, is contacted with the test agent, and is measured for effects of the test agent (abstract). The method is used to screen for therapeutic agents (abstract).

Kai does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc³ aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Kai using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture

Art Unit: 1651

practices in the art to culture the cartilage of Kai via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures.

Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

4. Claims 1 – 10, 14, 17 – 26, 33 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Purchio in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is capable of being rapidly degraded losing about half of its proteoglycan content within 24 hours when treated with IL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan,

Art Unit: 1651

collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc³ aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring comprises measuring the amount of proteoglycan in the ECT, is performed without addition of extrinsic radioactivity and the method further comprises identifying one or more test agents that have desirable characteristics and producing the agents as a therapeutic drug. The culturing of ECT and the contacting the cells with the test agent occurs in the same well of a multi-well plate.

Purchio teaches methods for screening effects of test agents on cartilage cultures wherein the cultures are exposed to the test agents and the effects are measured (col.16 line 12-22). Examples of such effects include the amount of proteoglycan (col.16 line 27-34). Specifically, chondrocytes are harvested from articular cartilage and cultured in multi-well plates (col.21 lines 18-60) and the test agents are identified for therapeutic and/or pharmaceutical compounds (col. 16). Purchio teaches that the chondrocytes can be isolated from articular or costal cartilage (col.11 line 62-65).

Purchio does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc³ aggrecan, a

Art Unit: 1651

ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Purchio using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Purchio via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures. Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

5. Claims 1 – 8, 17 – 24, 29 – 30 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Saito in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the

Art Unit: 1651

agents have on the ECT or cells thereof; wherein the matrix is capable of being rapidly degraded losing about half of its proteoglycan content within 24 hours when treated with IL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc³ aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium. The modulator of the ECT tissue is a matrix stimulating agent, cytokine or TNF-alpha wherein the cytokine is interleukin 1 (IL-1). Finally, the culturing and contacting step occur in the same well of a multi well plate.

Saito teaches culturing cartilage in multi well plates in the presences of IL-1 alpha, wherein the effects of the test agent were measured (p.727).

Art Unit: 1651

Saito does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc3 aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Saito using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Saito via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures.

Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

6. Claims 1 – 11, 17 – 27 and 29 – 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huch in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is capable of being rapidly degraded losing about half of its proteoglycan content within 24 hours when treated with IL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II, IX, XI, hyaluronan, and at least about 5 mg/cc³ aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring comprises measuring the amount of proteoglycan in the ECT, enzymatically degrading the ECT and is performed without addition of extrinsic radioactivity. The method further comprises identifying one or more test agents that have desirable

Art Unit: 1651

characteristics and producing the agents as a therapeutic drug. The culturing of ECT and the contacting the cells with the test agent occurs in the same well of a multi-well plate. The modulator of the ECT tissue is a matrix stimulating agent, cytokine or TNF-alpha wherein the cytokine is interleukin 1.

Huch teaches methods for culturing articular chondrocytes in an alginate medium in the presence of a test agent, IL-1, wherein proteoglycan was measured (abstract). Specifically, the cartilage was degraded with enzymes, the chondrocytes were cultured with alginate in a multi-well plate in the presence of IL-1, and the amount of proteoglycan was measured (p. 2158).

Huch does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc3 aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to culture the cartilage of Huch using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Huch via the methods of Masuda with a reasonable

Art Unit: 1651

expectation for successfully determining the effects of test agents on cartilage cultures.

Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

7. Claims 1 – 8, 10, 14, 17 – 24, 26 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lansbury in view of Masuda.

Applicant claims a method for determining the effect of a test agent on a tissue engineered cartilage matrix, the method comprising culturing an engineered cartilage tissue (ECT), contacting test agents with cells or tissues of the ECT, and measuring the effect that the agents have on the ECT or cells thereof; wherein the matrix is capable of being rapidly degraded losing about half of its proteoglycan content within 24 hours when treated with IL-1. The ECT is cultured by culturing isolated chondrogenic cells for a time sufficient to form a chondrogenic cell-associated matrix, and culturing the cells with the cell-associated matrix on a semipermeable membrane in the presence of a growth factor for a time sufficient to form an ECT. The cells or tissues are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT. Alternatively, the cells are selected from isolated chondrogenic cells, the chondrogenic cells during culture, the cells and cell-associated matrix before or after culturing, and the ECT in the presence of a known modulator of cartilage tissue. The chondrogenic cell-associated matrix comprises aggrecan, collagen types II, IX, XI, matrix proteins, and hyaluronan and the ECT comprises collagens II,

Art Unit: 1651

IX, XI, hyaluronan, and at least about 5 mg/cc³ aggrecan, the ratio of aggrecan : hyaluronan is about 10:1 – 200:1, and the ration of aggrecan : collagen is about 1:1 – 10:1. The isolated chondrogenic cells are isolated from articular cartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoids or cricoid cartilages, specifically fibrocartilage from ligament, tendon, meniscus, or intervertebral disc. The chondrogenic cells are cultured on an alginate medium, the measuring is performed without addition of extrinsic radioactivity and the method further comprises identifying one or more test agents that have desirable characteristics and producing the agents as a therapeutic drug.

Lansbury teaches methods for screening the effects of agents on cartilage cultures wherein a chondrocyte cell culture is incubated (or contacted) with the test agent and the effects are measured (claim 34). The method is used to identify agents with desirable, therapeutic characteristics, specifically the ability to repair damaged cartilage (claim 34).

Lansbury does not teach the method wherein the cartilage is cultured in the manner claimed. However, Masuda teaches methods for culturing an engineered cartilage tissue, wherein isolated chondrocytes are cultured in alginate for a time to allow a cell associated matrix to form (col.4 line 30-35). The cell associated matrix has at least about 5 mg/cc³ aggrecan, a ratio of aggrecan to hyaluronan of 10:1 to 200:1, and a ratio of aggrecan to collagen of about 1:1 to 10: (col.4 line 35-40). The chondrogenic cells are cultured on a semi-permeable membrane in the presence of growth factors (col. 4 line 44-46). The chondrocytes may be isolated from articular cartilage, fibrocartilage, costal, nasal, auricular, tracheal, epiglottic, thyroid, arytenoid or cricoid cartilages (col.5 line 31-38) and the resulting matrix comprises aggrecan, collagn II, IX, XI and hyaluronan (col.6 line 61-64). At the time of the claimed invention, it would have

Art Unit: 1651

been obvious to one of ordinary skill in the art to culture the cartilage of Lansbury using the methods of Masuda because it was a known method for culturing cartilage tissues. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by common culture practices in the art to culture the cartilage of Lansbury via the methods of Masuda with a reasonable expectation for successfully determining the effects of test agents on cartilage cultures. Although Masuda does not teach the fibrocartilage is from a ligament, tendon, meniscus or intervertebral discs, they were each well known sources of fibrocartilage. Moreover at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to use any of the above sources as the source of fibrocartilage in the methods of Masuda.

Response to Arguments

Applicant argues the cited references do not teach the matrix wherein it can be rapidly degraded upon treatment with IL-1, stating that such advantages are useful for high throughput screening of compounds and that the references do not recognize such advantages of the matrix.

However these arguments fail to persuade because although the references do not specifically teach the intrinsic property of the matrix, such attributes are inherent to the matrix of Masuda. Since the matrix of Masuda is the same as the presently claimed matrix, it would appear that the undisclosed property is also characteristic of the matrix disclosed by Masuda. Moreover, mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention (MPEP 2145).

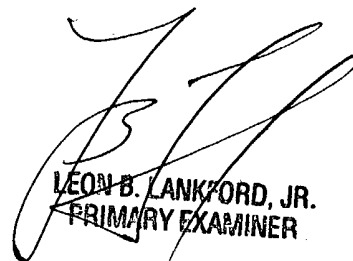
Art Unit: 1651

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 571-272-0915. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ruth A. Davis; rad
April 28, 2004.



LEON B. LANKFORD, JR.
PRIMARY EXAMINER